NON-SCIENTIFIC ABSTRACT

Non-Technical Abstract

Colorectal cancer (CRC) afflicts approximately 150,000 patients per year in the United States, with greater than 40% of these patients destined to die of the disease, despite current medical management. Death is commonly due to progressive cancer growth in the liver, which eventually affects liver function. Hepatocellular cancer (HCC) strikes approximately 8,000 patients per year in the United States and about 1.25 million worldwide. Unfortunately, most patients with these liver tumors cannot be cured with existing medical treatment. General expectancy for survival of CRC patients after diagnosis with liver metastases, and for HCC patients, is poor.

The human p53 gene is called a tumor suppressor gene because it is believed to prevent normal cells from developing into cancer cells. When the p53 gene becomes altered (such as by loss or mutation) this helps cancers to form. The p53 gene is frequently altered in the tumors of patients with CRC and HCC. In scientific experiments using cells in the test tube and in animals, introducing a normal copy of the p53 gene into cancer cells that have abnormal p53 can cause the cancer cells to grow more slowly, stop growing, or die.

ACN53 is a new gene therapy that contains the p53 gene in a modified virus. The virus is used to deliver the copy of the gene into the malignant tumor cells. The modified virus has been constructed from an adenovirus most frequently associated with the common cold. The virus has been modified so that the parts of the virus necessary to reproduce itself have been deleted and in turn are replaced by the p53 gene. It is not expected that the resultant virus will be able to multiply in the patient. The purpose of the study is to determine if the use of ACN53 in patients is safe. The study will also collect information to see if the reintroduction of the normal p53 gene into malignant liver tumors that are p53-altered can cause the tumors to grow more slowly, stop growing, or die. ACN53 will be given to patients with CRC spread to the liver or with HCC, by a single dose injection into a major blood vessel leading to the liver. There are two major blood vessels leading to the liver. The blood vessel selected for injection of ACN53 is the vessel most likely to supply liver tumors with blood necessary for their growth. The trial will study the safety and effect of different dose levels of ACN53 using this new therapy. The maximum number of patients expected to be involved in this study is 27. Only those patients who have evidence of abnormal p53 in their liver tumors can enroll in the study, thereby, selecting those patients who may potentially benefit from this gene replacement therapy.